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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/502,255	03/28/2005	Giuseppe Alvaro	PI4747USW	3929

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EXAMINER	
JOHNSEN, JASON H	

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 11/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/502,255	ALVARO ET AL.	
	Examiner	Art Unit	
	Jason H. Johnsen	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,15 and 17-66* is/are pending in the application.

4a) Of the above claim(s) *22-25,31-34,37,38,40,41 and 43-66* is/are withdrawn from consideration.

5)☒ Claim(s) *1-11,15 and 17-21* is/are allowed.

6)☒ Claim(s) *26-30,35,36,39 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *N/A* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/31/05,7/22/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d) filed on 02/08/2002.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 07/22/04 and 05/31/05 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the examiner is considering the information disclosure statements.

Election/Restriction

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-11, 15, 17-21, 26-30, 35, 36, 39, 42, and 61-66 drawn to compounds of formula I, the compositions, and methods of use relating to CNS disorders selected from depressive states and anxiety.

Group II, claim(s) 22-25, drawn to method for treatment of a condition mediated by a tachykinin.

Group III, claim(s) 31-34, drawn to combination therapies for treatment of a CNS disorder, further administering a serotonin reuptake inhibitor or a dopaminergic antidepressant.

Group IV, claim(s) 37, 38, 40, 41, drawn to combination therapies for the treatment of a major depressive disorder, and anxiety further administering a serotonin reuptake inhibitoror a dopaminergic antidepressant.

Group V, claim(s) 44-58 drawn to methods for treating emesis.

Group VI, claim(s) 59 drawn to a method for treating sleep disorders.

Group VII, claim(s) 60 drawn to a method for treating dependence on a substance.

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.

A telephone call was made to Ms. Lorie Ann Morgan on Monday October 3rd, 2005, which resulted in an election of group I.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 26-30, 35, 36, 39, and 42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Regarding claims 26 and 30, The origin and the nature of many **central nervous system disorders** (CNS) such as Depression, Meningitis (viral, bacteria, or fungi infection), Encephalitis (viral infection), Rett syndrome, Tinnitus, Narcolepsy, Shy-Drager syndrome, Charcot-Marie-Tooth disease, Tarsal tunnel syndrome, Psychosis, Memory loss, Mental retardation, Autism, Migraine, Tension headache, Multiple sclerosis, etc are different one from the other. The symptoms and nature of these diseases are also different one from the other. Some CNS disorders are hereditary (Charcot-Marie-Tooth disease). Many CNS disorders vary in how they affect the body and its functions. Diseases such as Cerebral palsy, and Parkinson's disease affect the movement of the patient. Diseases such as Alzheimer's disease affect the memory of the patient. Since the origin and nature of CNS disorders vary extremely one from the other, it is impossible to treat central nervous system disorders in general.

Regarding the more specific central nervous disorders found in claims 27, 28, 29, 35, 36, 39, and 42. Claims 27, 28, 29, 35, 36, 39, and 42 teach a method of treating a CNS disorder selected from depressive states and anxiety, more specific depressive states selected from the list in claim 28, more specific CNS disorders selected from the list in claim 29, major depressive disorder, including bipolar depression and unipolar depression of claim 36. These claims also teach treatment of anxiety and panic disorder by administering compounds of claim 1 broadly, and more specific species found in claims 35, 39, and 42. The specification discloses examples of measuring NK1-receptor binding affinity in vitro by measuring the compounds ability to displace (3H)-substance P from recombinant human NK1 receptors expressed in Chinese

Hamster Ovary cell membranes and from gerbil and marmoset brain cortex homogenates. However, applicant gives no actual experimental data using these methods to treat a disease state involving a CNS disorders broadly, depressive states broadly, anxiety broadly, or some of the more specific depressive states and anxiety listed in these claims. Applicant only has biological data drawn to substance P and compounds that are antagonists of the NK1 receptor. However, there are three main tachykinins that act as neurotransmitters and neuromodulators--substance P, Neurokinin A and Nuerokinin B. Applicant does not have biological data regarding Neurokinin A or B. Furthermore, there are three main tachykinin receptors, NK1, NK2 and NK3. Again, applicant does not provide biological data regarding NK2 or NK3 sufficient for one of ordinary skill to extrapolate that Applicant's claimed compounds are useful in treating CNS disorders, depressive states and anxiety relating to these neurotransmitters and their respective receptors. In addition, the specification fails to provide any evidence that the entire scope of the instantly claimed genus's would be effective *in vitro*, let alone *in vivo*, for the claimed treatments. Note that in cases involving physiological activity, "the scope of enablement varies inversely with the degree of unpredictability of the factors involved." *In re Fisher,* 427 F.2d 833, 166 USPQ 18 (CCPA 1970). Since this case involves unpredictable *in vitro* and *in vivo* physiological enzyme inhibition activities, any evidence presented must be commensurate in scope with the claims and must clearly demonstrate the effectiveness of the claimed compounds. The instant application provides no such evidence.

Furthermore, the instant specification provides no direction or guidance for how to use the disclosed (and claimed) compounds since there are no guidelines for determination of dosage needed to provide the inhibitory effect and no teaching or date provided which would permit the

determination of an effective amount for treating these disorders. Therefore, in view of the breadth of the claims, the chemical nature of the invention, the unpredictability of *in vitro* and *in vivo* correlation, the lack of any working examples, and the lack of any guidance in how to use the claimed compounds and compositions to actually treat these disorders, it would require an undue amount of experimentation to use the claimed inventions.

ALLOWABLE SUBJECT MATTER

The subject matter found in claims 1-11, 15, 17-21 is allowable for the following reason(s): The primary reason for the allowance of the claims is the inclusion of the limitation for R6 or R7, providing one or the other is a radical of formula (W). These technical features are seen to be free from the prior art and these limitations are not taught or fairly suggested by the prior art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jason H. Johnsen** whose telephone number is **571-272-3106**. The examiner can normally be reached on Mon-Friday, 8:30-5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Thomas Charles McKenzie

THOMAS CHARLES MCKENZIE
PATENT EXAMINER

Jason H. Johnsen
Patent Examiner
Art Unit 1623

James O. Wilson
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